

## Gene Section

### Mini Review

# HBP1 (HMG-box transcription factor 1)

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Published in Atlas Database: March 2009

Online updated version: <http://AtlasGeneticsOncology.org/Genes/HBP1ID40791ch7q22.html>

DOI: 10.4267/2042/44683

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## Identity

**Other names:** FLJ16340

**HGNC (Hugo):** HBP1

**Location:** 7q22.3

**Local order:** The HBP1 gene is located between the PRKAR2B gene (left) and the COG5 gene (right).

## DNA/RNA

### Description

Sequence length 33515; cDNA length 2829; Coding sequence 1545. The gene is comprised of 11 exons; max. exon length 1121, min. exon length 54. Number of SNPs 6.

### Transcription

The consensus normal transcript is 2829 nt and the coding sequence is 1545 nt. The consensus normal transcript is produced from 11 exons. The first exon is non-coding. There are 16 different mRNAs produced, including 13 different alternatively spliced variants. Several of these alternatively spliced variants appear to be produced only in tumor cells.

## Pseudogene

None known.

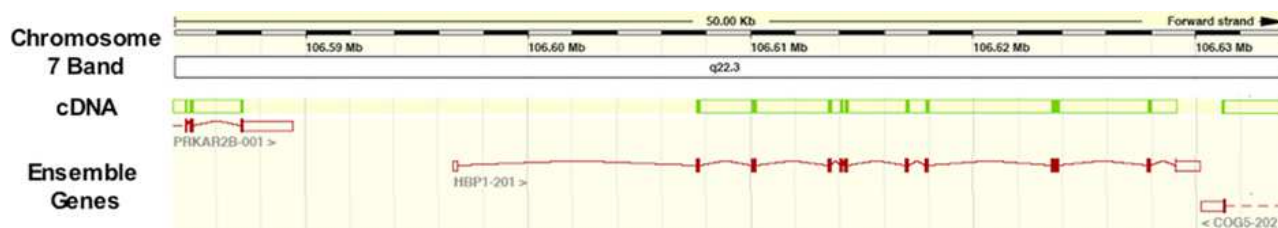
## Protein

### Description

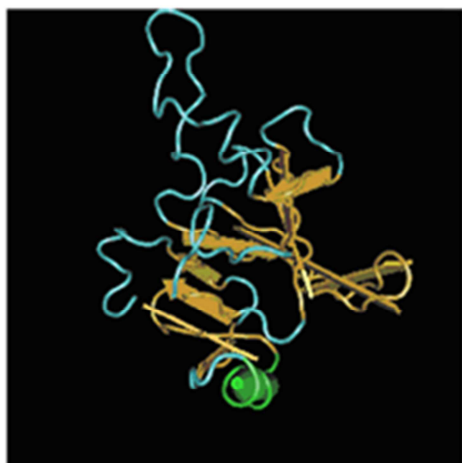
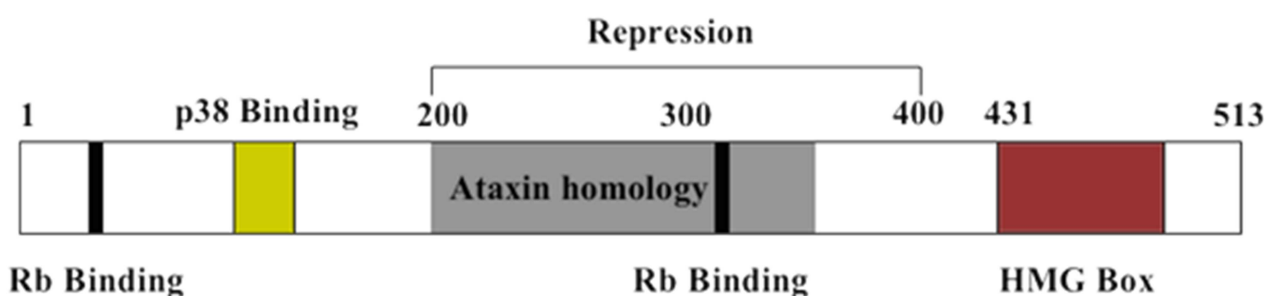
HBP1 encodes a 515 amino acid, 62-kDa, transcriptional repressor. On western blots, HBP1 runs anomalously at 75 kD. HBP1 represses numerous target genes when overexpressed, including N-Myc, cyclin D1 and c-myc. The protein contains two known domains: an HMG box DNA binding domain and a repression domain that contains an ataxin homology domain.

### Expression

HBP1 mRNA is expressed in several human organs and tissues: brain; uterus; testis; mixed; uncharacterized tissue; lung; bladder; kidney; heart; lymph node; blood; prostate; trachea; esophagus; cervix; skin; adrenal gland; eye; intestine; vascular; amniotic fluid; mouth; embryonic tissue; spleen; thymus; placenta; connective tissue; liver; mammary gland; muscle; pancreas; stomach; ovary; ascites; ganglia; bone; pharynx; thyroid; adipose tissue; parathyroid; ear; pineal gland; nerve; bone marrow; umbilical cord.



HBP1 Locus on 7q22. Chromosome 7, band q22 is shown at the top of the diagram with the distance on the forward strand marked as indicated. The HBP1 gene is located between the PRKAR2B gene (left) and the COG5 gene (right). Coding exons are shown in bold red, while non-coding are shown with open red boxes. cDNA coding sequence is shown in dark green.



## HBP1 Ataxin homology domain

HBP1 Protein Schematic. HBP1 contains two defined domains; an ataxin homology domain (gray) and an HMG box DNA binding domain (red). There are two Rb-interacting motifs (black line) and a p38 MAP kinase-interacting region (yellow). A repression domain (aa200-400) encompasses the Ataxin homology domain.

### Localisation

HBP1 is predominantly a nuclear protein.

### Function

**Cell Cycle.** HBP1 was isolated as a cell cycle inhibitor and HMG-box transcriptional repressor. HBP1 binds to Rb and p107 via an LXCXE and IXCXE binding motif as part of HBP1 function in cell cycle regulation. HBP1 expression was uniquely associated with oncogene-mediated senescence in an RB-dependent manner.

**Growth and Differentiation.** Liver-specific expression of HBP1 was shown to inhibit liver regeneration. In addition, ectopic expression of HBP1 regulates differentiation in muscle cells. Similarly, transgenic mice overexpressing HBP1 exhibited altered thymus cellularity and decreased thymocyte development. Finally, HBP1 expression is maintained in the developing testis beyond the onset of spermatogenesis, and the expression of HBP1 in XY germ cells appears to correlate with the onset of mitotic arrest. The repression domain of HBP1 contains an Ataxin homology domain which interacts with the Sin3 corepressor PAH2 domain, thus recruiting HDAC1 to a repression complex.

**Signaling and Transcription.** HBP1 inhibits a number of genes through direct binding to its cognate recognition sequence, including N-myc and p47 phox.

In addition, HBP1 is an inhibitor of Wnt signaling and blocks beta-catenin/LEF/TCF complexes. Wnt target genes regulated by HBP1 include c-myc and cyclin D1. HBP1 is regulated by p38 MAP kinase signaling and contains both a p38 MAP kinase docking sequence and a p38 MAP kinase phosphorylation site. Phosphorylation results in HBP1 protein stabilization and increased repression function. p38 MAP kinase phosphorylation is also required for HBP1 induction of premature senescence. HBP1 mRNA is stabilized by the green tea compound epigallo-catechin galate (EGCG), resulting in increased HBP1 protein and HBP1-dependent repression of Wnt signaling.

### Homology

HBP1 contains two recognized homology motifs; an Ataxin homology domain and an HMG box DNA binding domain.

## Mutations

### Somatic

In an analysis of 76 breast tumors, 10 HBP1 mutations/variants were identified that were associated with fully invasive breast cancer. Some of these mutants/variants were shown to be the result of genomic mutations.

## Implicated in

### Breast Cancer

#### Disease

Aberrations in HBP1 are associated with invasive breast cancer. The HBP1 gene is either mutated or reduced in breast cancer. As cited above in the "Somatic Mutation section", HBP1 mutations/ variants were associated with fully invasive breast cancer, some of which arose from genomic mutations. In a new analysis, a subset of invasive breast cancer tumors had markedly reduced expression of the HBP1 mRNA.

#### Prognosis

Statistical analysis of a breast cancer patient database predicted that reduced HBP1 mRNA levels were associated with a decreased relapse-free survival and recurrence with distant metastases (Paulson et al., 2007).

## References

Lavender P, Vandel L, Bannister AJ, Kouzarides T. The HMG-box transcription factor HBP1 is targeted by the pocket proteins and E1A. *Oncogene*. 1997 Jun 5;14(22):2721-8

Tevosian SG, Shih HH, Mendelson KG, Sheppard KA, Paulson KE, Yee AS. HBP1: a HMG box transcriptional repressor that is targeted by the retinoblastoma family. *Genes Dev*. 1997 Feb 1;11(3):383-96

Gartel AL, Goufman E, Tevosian SG, Shih H, Yee AS, Tyner AL. Activation and repression of p21(WAF1/CIP1) transcription by RB binding proteins. *Oncogene*. 1998 Dec 31;17(26):3463-9

Shih HH, Tevosian SG, Yee AS. Regulation of differentiation by HBP1, a target of the retinoblastoma protein. *Mol Cell Biol*. 1998 Aug;18(8):4732-43

Zhuma T, Tyrrell R, Sekkali B, Skavdis G, Saveliev A, Tolaini M, Roderick K, Norton T, Smerdon S, Sedgwick S, Festenstein R, Kioussis D. Human HMG box transcription factor HBP1: a role in hCD2 LCR function. *EMBO J*. 1999 Nov 15;18(22):6396-406

Lemercier C, Duncliffe K, Boibessot I, Zhang H, Verdel A, Angelov D, Khochbin S. Involvement of retinoblastoma protein and HBP1 in histone H1(0) gene expression. *Mol Cell Biol*. 2000 Sep;20(18):6627-37

Sampson EM, Haque ZK, Ku MC, Tevosian SG, Albanese C, Pestell RG, Paulson KE, Yee AS. Negative regulation of the Wnt-beta-catenin pathway by the transcriptional repressor HBP1. *EMBO J*. 2001 Aug 15;20(16):4500-11

Shih HH, Xiu M, Berasi SP, Sampson EM, Leiter A, Paulson KE, Yee AS. HMG box transcriptional repressor HBP1 maintains a proliferation barrier in differentiated liver tissue. *Mol Cell Biol*. 2001 Sep;21(17):5723-32

de Chiara C, Giannini C, Adinolfi S, de Boer J, Guida S, Ramos A, Jodice C, Kioussis D, Pastore A. The AXH module: an independently folded domain common to ataxin-1 and HBP1. *FEBS Lett*. 2003 Sep 11;551(1-3):107-12

Xiu M, Kim J, Sampson E, Huang CY, Davis RJ, Paulson KE, Yee AS. The transcriptional repressor HBP1 is a target of the p38 mitogen-activated protein kinase pathway in cell cycle regulation. *Mol Cell Biol*. 2003 Dec;23(23):8890-901

Berasi SP, Xiu M, Yee AS, Paulson KE. HBP1 repression of the p47phox gene: cell cycle regulation via the NADPH oxidase. *Mol Cell Biol*. 2004 Apr;24(7):3011-24

Smith JM, Bowles J, Wilson M, Koopman P. HMG box transcription factor gene Hbp1 is expressed in germ cells of the developing mouse testis. *Dev Dyn*. 2004 Jun;230(2):366-70

Swanson KA, Knoepfler PS, Huang K, Kang RS, Cowley SM, Laherty CD, Eisenman RN, Radhakrishnan I. HBP1 and Mad1 repressors bind the Sin3 corepressor PAH2 domain with opposite helical orientations. *Nat Struct Mol Biol*. 2004 Aug;11(8):738-46

Yee AS, Paulson EK, McDevitt MA, Rieger-Christ K, Summerhayes I, Berasi SP, Kim J, Huang CY, Zhang X. The HBP1 transcriptional repressor and the p38 MAP kinase: unlikely partners in G1 regulation and tumor suppression. *Gene*. 2004 Jul 7;336(1):1-13

de Chiara C, Menon RP, Adinolfi S, de Boer J, Ktistaki E, Kelly G, Calder L, Kioussis D, Pastore A. The AXH domain adopts alternative folds the solution structure of HBP1 AXH. *Structure*. 2005 May;13(5):743-53

Sekkali B, Szabat E, Ktistaki E, Tolaini M, Roderick K, Harker N, Patel A, Williams K, Norton T, Kioussis D. Human high mobility group box transcription factor 1 affects thymocyte development and transgene variegation. *J Immunol*. 2005 Oct 15;175(8):5203-12

Kim J, Zhang X, Rieger-Christ KM, Summerhayes IC, Wazer DE, Paulson KE, Yee AS. Suppression of Wnt signaling by the green tea compound (-)-epigallocatechin 3-gallate (EGCG) in invasive breast cancer cells. Requirement of the transcriptional repressor HBP1. *J Biol Chem*. 2006 Apr 21;281(16):10865-75

Zhang X, Kim J, Ruthazer R, McDevitt MA, Wazer DE, Paulson KE, Yee AS. The HBP1 transcriptional repressor participates in RAS-induced premature senescence. *Mol Cell Biol*. 2006 Nov;26(22):8252-66

Paulson KE, Rieger-Christ K, McDevitt MA, Kuperwasser C, Kim J, Unanue VE, Zhang X, Hu M, Ruthazer R, Berasi SP, Huang CY, Giri D, Kaufman S, Dugan JM, Blum J, Netto G, Wazer DE, Summerhayes IC, Yee AS. Alterations of the HBP1 transcriptional repressor are associated with invasive breast cancer. *Cancer Res*. 2007 Jul 1;67(13):6136-45

Shilo S, Roy S, Khanna S, Sen CK. Evidence for the involvement of miRNA in redox regulated angiogenic response of human microvascular endothelial cells. *Arterioscler Thromb Vasc Biol*. 2008 Mar;28(3):471-7

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*This article should be referenced as such:*

Paulson KE, Yee AS. HBP1 (HMG-box transcription factor 1). *Atlas Genet Cytogenet Oncol Haematol*. 2010; 14(2):124-126.

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